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10/538,931	06/14/2005	Jeffrey MICHAEL Axten	P51403	6740

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
08/12/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary	Application No.	Applicant(s)	
	10/538,931	AXTEN ET AL.	
	Examiner	Art Unit	
	/Venkataraman Balasubramanian/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response, which included addition of new claims 14-22 and amendment to claims 1, 3, 11 and 13, filed on 4/30/2008, is made of record. Claims 1-22 are now pending. In view of applicants' response, the following rejections made in the previous office action are maintained. I*n addition, a new ground of rejection is applied to claim 13.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating bacterial infections due to the panel of Gram-positive organisms consisting of: Staphylococcus aureus WCUH29, Streptococcus pneumoniae 1629, Streptococcus pyrogenes CN 10, Enterococcus faecalis 2, and a panel of Gram-negative organisms consisting of: Haemophilus influenzae NEMC1, E. coli 7623 and Moraxella catarrthalis Ravasio, does not reasonably provide enablement for any or all bacterial infections The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Following reasons apply.

The instant claim 13 is drawn to "treating any or all bacterial infection". Instant claims, as recited, are reach through claims. A reach through claim is a claim drawn to a

mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the inhibition of growth of a panel of by the instant compounds, claim 13 reaches through treating any or all bacterial infections in general and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as inhibitor of growth of a panel of bacteria, based on limited assay, it is claimed that treating any or all bacterial infections in general. The scope of the claims includes not only any or all bacterial infections for which there is no enabling disclosure.

The scope of the claims includes treating any or all bacterial infections which is not adequately enabled solely based on the activity of the compounds provided in the specification at pages 211-212. The instant compounds are disclosed to have bacterial inhibitory activity due to the mode of action as growth inhibitors and it is recited that the instant compounds are useful in treating bacterial infection, for which applicants provide no competent evidence. The fact that a single class of compounds can be used treat any or all bacterial infections is new finding for which there is no support in the prior art.

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed treating of any or bacterial infections solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Snyder et al., J. Med. Liban 48(4): 208-214, 2000 (PubMed Abstract provided), wherein with regards to antibacterial therapies, it is stated that " common bacteria whose susceptibility to antimicrobials is no longer predictable". Note also that despite the fact there are several commercial antibacterial agents are available, it is still difficult to treat several pathogens such as those cause leprosy, meningitis, sexually transmitted infections, anthrax etc.

No compound has ever been found that can control or treat bacterial infections generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. Nearly all drugs for treating infections are effective against only a limited group of disorders. Therefore, a compound effective against all bacterial infection generally would be a revolutionary exception. It is well established that an enablement rejection is proper when the scope of enablement is not reasonably correlated to the scope of the claims. (In re Vaeck, 20 USPQ2d 1439, 1444 (CAFC 1991); In re Ferens, 163 USPQ 609).

It is inconceivable as to how the claimed compounds can treat all types of bacterial infections for which applicants provide no competent evidence. For example,

there is no common mechanism by which all bacterial infectious conditions arise. Accordingly, treatments for these diseases are normally tailored to the particular type of microorganism or infection present and there is no 'magic bullet' against infections in general. There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) due to such infections. The test example in the specification indicates specific types of Gram-positive and Gram-negative organisms (see pages 211-212).

There is no evidence in the record which demonstrates that the screening test relied upon are recognized in the art as being reasonably predictive of success in any of the contemplated areas of 'therapeutic treatment' of all types of bacterial infections. Such a reasonable correlation is necessary to demonstrate such utilities. See Ex parte Stevens, 16 USPQ 2d 1379 (BPAI 1990); Ex parte Busse et al., 1 USPQ 2d 1908 (BPAI 1986) (the evidence must be accepted as "showing" such utility and not "warranting further study"). The evidence presented in this case does not show such utilities, but only warrants further study.

Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.". Clearly that is the case here.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating bacterial infections.

2) The state of the prior art: A recent publication expressed that the antibacterial effects of bacterial inhibitors are unpredictable.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating any or all bacterial infections by the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all bacterial infections and the state of the art is that the effects of bacterial inhibitors are unpredictable.

6) The breadth of the claims: The instant claims embrace treatment of bacterial infections with a large genus of compounds embraced in claim 1.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of bacterial infections of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-22 are rejected under 35 U.S.C. 103(a) as being obvious over Davies et al., US 6,962,917 (or WO 02/08224).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Davies et al., teaches several aminopiperidine compounds which include instant compounds for the same use. See column 1, formula I. Note when Z^1 and Z^5 are CR^{1a}, with the given definition of various variable groups, compounds taught by Davies et al., include instant compounds. See entire document, especially column 1-21 for various preferred embodiments and process of making these compounds. See column 21-56 for examples 1-625.

Davies et al., differs from instant claims in not exemplifying compounds wherein Z^5 is C-halogen. However, Davies et al., teaches equivalency of those compounds

wherein Z^5 is CH with those generically claimed for formula I. Thus, it would be obvious to one trained in the art to make compounds taught by Davies et al., including those bearing Z^5 = C-halogen, and expect these compounds to have the use taught therein in view of the equivalency teachings outlined above.

This rejection is same as made in the previous office action but now includes newly added claims 14-22. Applicants' traversal is not persuasive.

Contrary to applicants' urging, Davies clearly permits R^{1a} to be halogen. See definition of R^{1a}. Thus , it is within the skill set of one trained in the art to make compound of formula I with variously substituted R^{1a}. Instant invention merely claims a subgenus of the compounds generically taught in the reference.

As for applicants' argument that Davies et al., teaching is limited to the embodiments of specific example, applicants' attention is drawn to In re Bruckel. Note In re Bruckel which states " References must be considered under 35 U.S.C 103, not only for what it expressly teaches but also for what it fairly suggests; all disclosures of prior art, including unpreferred embodiments must be considered in determining obviousness". In re Bruckel, 201 USPQ 67.

Also see KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727 (2007), wherein the court stated that

[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill

and common sense.

Such is the case with instant claims. Davies et al., teaches genus of compounds which include instant compounds and exemplifies large number of compounds include fluoro and trifluoromethyl substituted piperidine bearing compounds stated above. Hence, based on the teaching that compounds taught, which provide guidance to choose the core and all the variables substituents taught therein including the various choices of R^{1a} as substituents on the quinoline, one trained in the art would be motivated to make compounds wherein the quinoline is substituted with various groups as permitted by R^{1a} choices including halogen. Such compounds are within the skill set of one trained in the art.

Hence, one trained in the art would be motivated to make variously substituted quinoline permitted by the reference and expect these compounds have the use taught for the exemplified compounds.

Hence, this rejection is proper and is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 7,312,212. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter namely the aminopiperidine compound of formula I, composition and the method of use as antibacterial gents embraced in the instant claims are also claimed in the claims of the said US patent. See claim 1 of US 7, 312,212 and note the overlapping of the subject matter claimed. See claim 2, wherein Z^5 is recited to be C-Cl. Also note several compounds with R^{1a} as fluoro are claimed. These are isomeric with the instant compounds. However, positional isomers are not deemed patentably distinct absent evidence of superior or unexpected properties. See In re Crounse, 150 USPQ 554; In re Norris 84 USPQ 458; In re Finely 81 USPQ 383 and 387; Ex parte Engelhardt, 208 USPQ 343; Ex parte Henkel, 130 USPQ 474, regarding positional isomers.

Thus it would have been obvious to one skilled in the art at the time of the invention was made to expect instant compounds to possess the utility taught by the applied art in view of the close structural similarity outlined above. Thus, it would be obvious to one trained in the art to make compounds generically claimed in claim based

on the exemplified species of claim 9, including those bearing C-halogen for Z^5 and expect these compounds to have the use taught therein.

This rejection is same as made in the previous office action but now includes newly added claims 14-22. Applicants' traversal is not persuasive.

Applicants have argued, after excluding halogen form R^3 definition, the instant R^3 is not taught in the claims of US 7,312,212. This is not entirely correct. Instant R^3 is permitted to be alkyl and specification clearly includes substituted alkyl as part of alkyl definition and the substituents recited for alkyl include halogen. Thus, trifluoromethyl taught in the said US patent is also included in the instant genus. In addition, R^3 is permitted to hydroxy and carboxy substituted group. See claim 1 of the said patent, last two lines of R^3 definition.

Hence, this rejection is proper and is maintained.

Claims 1-13 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,962,917. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter namely the aminopiperidine compound of formula I, composition and the method of use as antibacterial gents embraced in the instant claims are also claimed in the claims of the said US patent. See claim 1 of US 6.962,917 and note the overlapping of the subject matter claimed. See teachings of above 103 rejection for further details. These are isomeric with the instant compounds. Thus, it would be obvious to one trained in the art to make compounds generically

claimed in claim based on the exemplified species of claim 9, including those bearing C-halogen for Z^5 and expect these compounds to have the use taught therein.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624